Clinical Policy: Asfotase Alfa (Strensiq)

Reference Number: PA.CP.PHAR.328
Effective Date: 01/2018
Last Review Date: 10/2024

Description
Asfotase alfa (Strensiq®) is a tissue nonspecific alkaline phosphatase.

FDA Approved Indication(s)
Strensiq is indicated for the treatment of patients with perinatal/infantile- and juvenile-onset hypophosphatasia (HPP).

Policy/Criteria
It is the policy of PA Health & Wellness® that Strensiq is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all):

1. Diagnosis of perinatal/infantile- or juvenile-onset hypophosphatasia (HPP) as evidenced by all of the following (a, b and c):
   a. Age of onset is < 18 years;
   b. Presence of one of the following laboratory indices (i or ii):
      i. Mutation in the ALPL gene encoding for tissue non-specific alkaline phosphatase (TNSALP)*;
      ii. Serum alkaline phosphatase (ALP) below the age-adjusted normal range and one of the following (1, 2 or 3):
         1) Plasma pyridoxal 5'-phosphate (PLP; main circulating form of vitamin B6) above the upper limit of normal (ULN) (measurement of plasma vitamin B6 requires stopping pyridoxine supplementation 1 week prior to measurement);
         2) Urinary phosphoethanoloamine (PEA) above the ULN;
         3) Plasma or urinary inorganic pyrophosphate (PPi) above the ULN;
   c. History of one of the following HPP clinical manifestations:
      i. Vitamin B6-dependent seizures;
      ii. Failure to thrive or growth failure/short stature;
      iii. Nephrocalcinosis with hypercalcemia/hypercalcuria;
      iv. Skeletal abnormalities and associated impairments (any of the following):
         a) Craniosynostosis (premature fusion of one or more cranial sutures) with increased intracranial pressure;
         b) Rachitic chest deformity (costochondral junction enlargement seen in advanced rickets) with associated respiratory compromise;
         c) Limb deformity with delayed walking or gait abnormality;
         d) Compromised exercise capacity due to rickets and muscle weakness;
         e) Low bone mineral density for age with unexplained fractures;
         f) Alveolar bone loss with premature loss of deciduous (primary) teeth;
2. Prescribed by or in consultation with an endocrinologist;
3. Prescribed dose does not exceed the following (a or b):

a. Perinatal/infantile-onset HPP: 9 mg/kg in split doses per week;
b. Juvenile-onset HPP: 6 mg/kg in split doses per week.

Approval duration: 6 months

**TNSALP is an ALP isoenzyme; a functional mutation in the gene (ALPL) encoding for TNSALP results in low TNSALP activity (as evidenced by a low serum ALP level) and increased levels of TNSALP substrates (PLP and PEA).*

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Perinatal/Infantile- and Juvenile-Onset Hypophosphatasia (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;;
2. Member is responding positively to therapy, as evidenced by improvement in any of the following on initial re-authorization request:
   a. Height velocity;
   b. Respiratory function;
   c. Skeletal manifestations (e.g., bone mineralization, bone formation and remodeling, fractures, deformities);
   d. Motor function, mobility, or gait;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Perinatal/infantile-onset HPP: 9 mg/kg per week;
   b. Juvenile-onset HPP: 6 mg/kg per week.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health &Wellness benefit or member has met all initial approval criteria or the Continuity of Care Policy (PA.PHARM.01) applies; **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to PA.CP.PHAR.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PHAR.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALP: alkaline phosphatase
FDA: Food and Drug Administration
HPP: hypophosphatasia
PEA: phosphoethanolamine
PLP: pyridoxal 5'-phosphate
PPi: inorganic pyrophosphate
TNSALP: tissue non-specific alkaline phosphatase
ULN: upper limit of normal

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): none reported

Boxed warning(s): hypersensitivity reactions including anaphylaxis

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Perinatal/infantile-onset HPP	6 mg/kg SC per week as either: • 2 mg/kg three times per week, or • 1 mg/kg six times per week The dose may be increased for lack of efficacy (e.g., no improvement in respiratory status, growth, or radiographic findings) up to 9 mg/kg per week, administered as 3 mg/kg SC three times per week.	9 mg/kg/week
Juvenile-onset HPP	6 mg/kg SC per week as either: • 2 mg/kg three times per week, or • 1 mg/kg six times per week	6 mg/kg/week

VI. Product Availability
Single-use vials: 18 mg/0.45 mL, 28 mg/0.7 mL, 40 mg/mL, 80 mg/0.8 mL

VII. References
1. Strensiq Prescribing Information. New Haven, CT: Alexion Pharmaceuticals, Inc.; July2024. Available at strensiq-hcp.com. Accessed July 15, 2024.
2. Beck C, Morback H, Stenzel M. Hypophosphatasia: Recent advances in diagnosis and treatment. Open Bone J. 2009; 1:8-15.
3. Scott LJ. Asfotase alfa in perinatal/infantile-onset and juvenile-onset hypophosphatasia: A guide to its use in the USA. Bio Drugs. 2016; 30:41-48. DOI 10.1007/s40259-016-0161-x.
4. Whyte MP, Rockman-Greenberg C, Ozono K, et al. Asfotase alfa treatment improves survival for perinatal and infantile hypophosphatasia. J Clin Endocrinol Metab. January 2016; 101(1):334-42. Doi: 10.1210/jc.2015-3462. Epub 2015 Nov 3.
5. Orimo H. Pathophysiology of hypophosphatasia and the potential role of asfotase alfa. Ther Clin Risk Manag. May 17, 2016; 12:777-86. Doi: 10.2147/TCRM.S87956. eCollection 2016.
6. Mornet E, Nunes ME. Hypophosphatasia. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. 2007 Nov 20 [updated 2016 Feb 4]. Available at https://www.ncbi.nlm.nih.gov/books/NBK1150/. Accessed August 30, 2017.
7. Bishop N. Clinical management of hypophosphatasia. Clin Cases miner Bone Metab. 2015; 12(2): 170-173.
8. Choida V, Bubbear JS. Update on the management of hypophosphatasia. Ther Adv Musculoskel Dis. 2019;11:1-8.
9. Kishnani PS, et al. Monitoring guidance for patients with hypophosphatasia treated with asfotase alfa. Mol Genetics and Metab. 2017;122:4-17.

10. Khan AA, Brandi ML, Rush ET, et al. Hypophosphatasia diagnosis: current state of the art and proposed diagnostic criteria for children and adults. Osteoporosis International. 2023;35:431-8. https://doi.org/10.1007/s00198-023-06844-1.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date
4Q 2018 annual review: no significant changes; added diagnosis confirmation and specialist requirements along with specific criteria for confirmation of positive response to therapy for renewals; references reviewed and updated.	07/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: Updated appendices and referenced reviewed and updated.	07/2020
4Q 2021 annual review: no significant changes; references reviewed and updated.	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: added elevated PPi level as an additional biochemical marker of decreased ALP activity based on the pathophysiology of HPP; added information regarding the need to stop pyridoxine supplementation one week prior to measuring plasma PLP to ensure accurate assessments of endogenous PLP levels; added new Boxed Warning from a recent label update; references reviewed and updated.	10/2024